

### **REMARKS/ARGUMENTS**

Claims 1-4, 6, 8-17, 19-21, and 23-24 are pending in this application and are presented for examination. Reconsideration is respectfully requested.

#### **I. INFORMATION DISCLOSURE STATEMENTS**

The Examiner has indicated that Applicants have not provided a copy of certain references cited in previous Information Disclosure Statements (IDS). In response, Applicants submit herewith a copy of each of the following references:

- (1) JP 3-127788 and JP 11349451, cited in the IDS dated January 24, 2005; and
- (2) JP 2-502822, JP 9-98447, JP 10-121876, JP 10-158782<sup>1</sup>, JP 9-188629, JP 10-265343, JP 9-5045387, JP 2810041<sup>2</sup>, Woodford *et al.* (from Purdue University, Vol. 66, No. 1, Jan. 1977), Abram *et al.* (from Mousses, Chapter 19, pp. 221-232), JP 64-68308, JP 64-68309, JP 64-68310, and JP 9-188620, cited in the IDS dated July 21, 2003.

In view of the foregoing, Applicants respectfully request that these references be considered by the Examiner.

#### **II. DOUBLE PATENTING REJECTION**

Claims 1-6, 8-9, and 12-19 were rejected under the judicially created doctrine of obviousness-type double patenting for allegedly not being patentably distinct over the claims of co-pending U.S. Patent Application No.10/124,197. In the Office Action, the Examiner has indicated that the double patenting rejection can be overcome by the filing of a Terminal Disclaimer (*see*, page 4 of the Office Action dated May 16, 2005).

Applicants have already filed a Terminal Disclaimer, which Terminal Disclaimer identifies the subject application in U.S. Patent Application No.10/124,197, which has now issued as U.S. Patent No. 6,946,120. As the subject application has already been identified in the Terminal Disclaimer filed in the earlier issued case, there is no reason to file yet another terminal

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<sup>1</sup> Applicants note that this reference is the application number of Publication No. 11-349451 cited in (1) above.

<sup>2</sup> Applicants note that this reference is equivalent to JP 64-68309 cited below.

disclaimer over the exact same application in the subject application. Accordingly, Applicants respectfully request that the Examiner withdraw this rejection.

### III. REJECTIONS UNDER 35 U.S.C. § 103(a)

#### A. Bazzano by itself or optionally in view of Weiner *et al.*

The Examiner has rejected claims 1-3, 6, 8-9, 12-17, 19, 21, and 23 as allegedly being obvious over Bazzano (U.S. Patent No. 5,183,817) by itself or optionally in view of Weiner *et al.* (WO 97/12602). In the Office Action, the Examiner states that the current claim language does not exclude the use of a retinoid as taught by Bazzano (*see*, page 7 of the Office Action dated May 16, 2005). The Examiner also states that it would have been obvious to one skilled in the art to modify the formulation of Bazzano to include an acid salt of minoxidil as taught by Weiner *et al.* (*see, Id.*, page 6). In response, Applicants respectfully traverse the rejection.

As set forth in M.P.E.P. § 2144.04:

[t]he omission of an element and retention of its function is an indicia of unobviousness. [Emphasis in original] *In re Edge*, 359 F.2d 896, 149 U.S.P.Q. 556 (CCPA 1966).

In this regard, the Examiner's attention is respectfully directed to column 5, lines 16-41, of Bazzano, which states the following:

[t]he present invention **combines** the use of retinoid compounds with minoxidil....While neither compound alone may have profound effects on advanced alopecias, **in combination** the compounds are very effective as promoters of new hair growth in areas of alopecia. The net result of application of minoxidil and retinoids is initiation and production of new hair growth and conversion of vellus to terminal hair growth....[T]his effect is obtained not merely as the addition of two compounds, but as synergism, i.e., the **combination** of these substances in the present invention produces an effect which cannot be produced by either compound separately under conditions of its use and, therefore, represents a major advance in the treatment of alopecia. [Emphasis added]

From the foregoing, it is clear that Bazzano teaches the **combined** use of minoxidil and a retinoid for promoting new hair growth. In fact, the retinoid is an essential

element of Bazzano because it ***must be combined*** with minoxidil in order to effectively treat alopecia. However, the present invention does not require that a retinoid be combined with minoxidil in order to effectively treat alopecia. Rather, the present invention promotes new hair growth by significantly increasing the solubility and concentration of minoxidil in the formulation. As a result, Applicants assert that the present invention omits an essential element of Bazzano (*i.e.*, a retinoid) while retaining its function (*i.e.*, promoting new hair growth). Thus, the present invention is unobvious in view of Bazzano.

In addition, Applicants respectfully remind the Examiner that to establish a *prima facie* case of obviousness, all the claim limitations must be taught or suggested by the prior art reference. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). As discussed above, Bazzano requires ***combining*** a retinoid with minoxidil for treating alopecia. However, Bazzano simply fails to teach or suggest the use of minoxidil ***without*** a retinoid. In essence, Bazzano only teaches the limitation of "minoxidil in combination with a retinoid," but ***not*** either component alone. In fact, Bazzano ***teaches away*** from the use of either compound alone by stating that "the ***combination*** of these substances in the present invention produces an effect which cannot be produced by either compound separately under conditions of its use and, therefore, represents a major advance in the treatment of alopecia" (Emphasis added; col. 5, lines 37-41). As a result, Applicants assert that Bazzano does not teach the limitation of "at least 5% by weight, based on the total weight of the composition, of minoxidil or a pharmaceutically acceptable salt thereof" set forth in claim 1 because Bazzano does not teach or suggest the use of minoxidil ***without*** a retinoid. As such, the present invention is unobvious in view of Bazzano.

Weiner *et al.* do not supply the deficiencies of Bazzano. In particular, Weiner *et al.* teach that minoxidil can be modified to make it more hydrophilic, for example, by converting it to an acid such as a lactic acid salt (*see*, page 4, lines 13-18). After the minoxidil has been made more hydrophilic, it ***must*** then be encapsulated in a lipid vesicle in order to achieve improved penetration through hair follicles (*see*, page 3, lines 5-10). However, Weiner *et al.* do not teach or suggest that its lipid vesicle formulations ***exclude*** the use of a retinoid. As a result, even if the formulation of Bazzano was modified to include an acid salt of minoxidil as taught by

Weiner *et al.*, one skilled in the art would have no motivation to modify the formulation by removing the requirement for a retinoid, which represents an essential element of Bazzano. Further, based upon the teaching of Bazzano that the **combination** of a retinoid and minoxidil is very effective at promoting new hair growth in areas of alopecia while neither compound alone has profound effects on advanced alopecias, one skilled in the art would have no reasonable expectation that modifying the formulation of Bazzano to include an acid salt of minoxidil **while removing** the requisite retinoid would be successful. In view of the foregoing, Applicants respectfully request that the Examiner withdraw the rejection.

B. Navarro *et al.* in view of Weiner *et al.*

The Examiner has rejected claims 1-4, 5-6, 8-9, 12-19, and 21-23 as allegedly being obvious over Navarro *et al.* (WO 95/25500) in view of Weiner *et al.* In the Office Action, the Examiner states that it would have been obvious to one skilled in the art to combine the teachings of these references and substitute the cyclodextrin of Navarro *et al.* (WO 95/25500) with the acid salt of minoxidil of Weiner *et al.* (see, page 9 of the Office Action dated May 16, 2005). The Examiner also states that Navarro *et al.* (WO 95/25500) teaches a hair composition containing 0.1% to 7% minoxidil (see, *id.*, page 8). However, Applicants would like to point out that this reference actually teaches a hair composition containing **0.1% to 3% minoxidil** (see, page 2, lines 19-25). Applicants respectfully submit that the Examiner may be referring to the teaching of the related Navarro *et al.* reference of record, WO 97/03638, which discloses the higher concentration of minoxidil. In any event, for the reasons discussed below, neither Navarro *et al.* alone, or in combination with Weiner *et al.* renders the present invention obvious.

Essentially, both Navarro *et al.* references ("Navarro *et al.*") teach encapsulating minoxidil in a cyclodextrin carrier, wherein cyclodextrin functions as a "host" molecule to trap the minoxidil "guest" molecule inside the ring. Navarro *et al.* also teach that the prior art use of solvents such as propylene glycol is to solubilize the active ingredient; however, the use of propylene glycol tends to give a greasy, shiny, and unattractive appearance to the hair upon application. In solving this prior art deficiency, Navarro *et al.* teach the use of cyclodextrin in

order to assist in the solubilization of minoxidil while avoiding high amounts of propylene glycol.

For example, Navarro *et al.* (WO 95/25500) sets forth:

[t]he amount of cyclodextrin present in the composition for hair is such that it permits a substantial reduction in the amount of solvent for minoxidil which would normally need to be added to achieve a comparable solubility of minoxidil in the absence of the aforementioned cyclodextrin. Page 2, lines 26-30.

Similarly, Navarro *et al.* (WO 97/03638) states the following:

[t]he amount of  $\gamma$ -cyclodextrin present in the composition for hair is such that it permits a substantial reduction in the amount of solvent for minoxidil which would normally need to be added to achieve a comparable solubility of minoxidil in the absence of the aforementioned cyclodextrin. Page 3, lines 9-13.

From the foregoing, it is clear that cyclodextrin is an essential element of Navarro *et al.* because it ***must be combined*** with minoxidil in order to impart improved solubility properties to minoxidil, thereby reducing the amount of solvent such as propylene glycol needed in the formulation. However, the present invention does not require that a cyclodextrin be combined with minoxidil in order to impart improved solubility properties to minoxidil while reducing the amount of propylene glycol needed in the formulation. Rather, the present invention significantly increases the solubility of minoxidil without the need of using large amounts of propylene glycol by adjusting the acid concentration in the formulation (see, page 2, lines 15-18). As a result, Applicants assert that the present invention omits an essential element of Navarro *et al.* (*i.e.*, a cyclodextrin) while retaining its function (*i.e.*, imparting improved solubility properties to minoxidil). M.P.E.P. § 2144.04. Thus, the present invention is unobvious in view of Navarro *et al.*

In addition, Applicants respectfully remind the Examiner that to establish a *prima facie* case of obviousness, all the claim limitations must be taught or suggested by the prior art reference. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). As discussed above, Navarro *et al.* requires ***combining*** a cyclodextrin with minoxidil, *i.e.*, forming a cyclodextrin-

minoxidil "host-guest" complex. However, Navarro *et al.* simply fails to teach or suggest the use of minoxidil **without** a cyclodextrin. In essence, Navarro *et al.* only teach the limitation of a "cyclodextrin-minoxidil complex," but **not** either component alone. In fact, Navarro *et al.* **teaches away** from the use of either compound alone by disclosing that it is the **combination** of these substances which imparts improved solubility properties to minoxidil while reducing the amount of solvent needed. As a result, Applicants assert that Navarro *et al.* do not teach the limitation of "at least 5% by weight, based on the total weight of the composition, of minoxidil or a pharmaceutically acceptable salt thereof" set forth in claim 1 because Navarro *et al.* do not teach or suggest the use of minoxidil **without** a cyclodextrin. As such, the present invention is unobvious in view of either of Navarro *et al.*

Weiner *et al.* do not supply the deficiencies of Navarro *et al.* In particular, Weiner *et al.* teach that minoxidil can be modified to make it more hydrophilic, for example, by converting it to an acid such as a lactic acid salt or by encapsulating it in cyclodextrin (*see*, page 3, lines 15-19). After the minoxidil has been made more hydrophilic, it must then be encapsulated in a lipid vesicle in order to achieve improved penetration through hair follicles (*see*, page 3, lines 5-10). According to the Examiner, one skilled in the art would have been motivated to substitute the cyclodextrin encapsulated minoxidil of Navarro *et al.* (WO 95/25500) with a lipid vesicle encapsulated minoxidil lactate because Weiner *et al.* compare the two formulations and shows that the lipid vesicle encapsulated minoxidil lactate affords better penetration (*see*, page 10 of the Office Action dated May 16, 2005). However, Applicants respectfully point out to the Examiner that such a substitution would destroy the aim of Navarro *et al.* In particular, the proposed modification that the Examiner contemplates would no longer follow the teaching of Navarro *et al.* that encapsulation of minoxidil by cyclodextrin is required in order to impart improved solubility properties to minoxidil.

Under MPEP § 2143.01, in making a *prima facie* case of obviousness, the Examiner's proposed modification **cannot** render the prior art unsatisfactory for its intended purpose:

If the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984).

In this case, the Examiner's proposed modification would eviscerate the primary aims of Navarro *et al.* and render the formulation unsatisfactory for its intended purpose. In fact, the modified formulation, which would contain the lipid vesicle encapsulated minoxidil lactate of Weiner *et al.* instead of the cyclodextrin encapsulated minoxidil of Navarro *et al.*, would destroy the objective of Navarro *et al.* of producing a lotion which is pleasant to use by formulating minoxidil within an inclusion complex of cyclodextrin. Further, in the absence of cyclodextrin, there would be insufficient penetration without the presence of high concentrations of propylene glycol, which tends to give a greasy, shiny, and unattractive appearance to the hair. Thus, the Examiner's proposed modification would create an unpleasant product that Navarro *et al.* is trying to avoid. In view of the foregoing, the withdrawal of the obviousness rejection is respectfully requested.

C. Bazzano in view of Weiner *et al.* and further in view of Uchikawa *et al.*

The Examiner has rejected claims 10-11, 20, and 24 as being allegedly obvious over Bazzano in view of Weiner *et al.* and further in view of Uchikawa *et al.* (U.S. Patent No. 5,156,836). In the Office Action, the Examiner states that it would have been obvious to one skilled in the art to combine the teachings of these references and substitute the ethanol solvent of Bazzano with the benzyl alcohol solvent of Uchikawa *et al.* (*see*, page 11 of the Office Action dated May 16, 2005). In response, Applicants respectfully traverse the rejection.

As discussed above, the present invention is unobvious in view of Bazzano and Weiner *et al.* Applicants assert that Uchikawa *et al.* do not supply the deficiencies of these references. In particular, Uchikawa *et al.* teach a composition for revitalizing hair that includes an amine oxide (*see*, col. 1, lines 55-57). Uchikawa *et al.* also disclose minoxidil and benzyl alcohol as part of a long list of general purpose components (*see*, col. 4, lines 7-33). However, Uchikawa *et al.* do not teach or suggest that its hair revitalizing compositions **exclude** the use of

a retinoid. As a result, even if the formulation of Bazzano was modified to include an acid salt of minoxidil as taught by Weiner *et al.* and a benzyl alcohol solvent as taught by Uchikawa *et al.*, one skilled in the art would have had no motivation to modify the formulation by removing the requirement for a retinoid, which represents an essential element of Bazzano. Further, based upon the teaching of Bazzano that the **combination** of a retinoid and minoxidil is very effective at promoting new hair growth in areas of alopecia while neither compound alone has profound effects on advanced alopecias, one skilled in the art would not have had any reasonable expectation that modifying the formulation of Bazzano to include an acid salt of minoxidil and a benzyl alcohol solvent **while removing** the requisite retinoid would be successful. In view of the foregoing, Applicants respectfully request that the Examiner withdraw the rejection.

D. Navarro *et al.* in view of Weiner *et al.* and further in view of Uchikawa *et al.*

The Examiner has rejected claims 10-11, 20, and 24 as allegedly being obvious over Navarro *et al.* in view of Weiner *et al.* and further in view of Uchikawa *et al.* In the Office Action, the Examiner states that it would have been obvious to one skilled in the art to combine the teachings of these references and substitute the ethanol solvent of Navarro *et al.* with the benzyl alcohol solvent of Uchikawa *et al.* (*see*, page 13 of the Office Action dated May 16, 2005). In response, Applicants respectfully traverse the rejection.

Again, Applicants would like to point out that Navarro *et al.* (WO 95/25500) actually teach a hair composition containing **0.1% to 3% minoxidil** (*see*, page 2, lines 19-25). Applicants respectfully submit that the Examiner may be referring to the teaching of the related Navarro *et al.* reference of record, WO 97/03638, which discloses the higher concentration of minoxidil. In any event, neither Navarro *et al.* reference alone, or in combination with Weiner *et al.* and Uchikawa *et al.* renders the present invention obvious.

As discussed above, the present invention is unobvious in view of Navarro *et al.* and Weiner *et al.* Applicants assert that Uchikawa *et al.* do not supply the deficiencies of these references. In particular, Uchikawa *et al.* teach a composition for revitalizing hair that includes an amine oxide (*see*, col. 1, lines 55-57). Uchikawa *et al.* also disclose minoxidil and benzyl



alcohol as part of a long list of general purpose components (*see*, col. 4, lines 7-33). However, Uchikawa *et al.* do not teach or suggest that its hair revitalizing compositions **exclude** the use of a cyclodextrin. As a result, even if the formulation of Navarro *et al.* was modified to include an acid salt of minoxidil as taught by Weiner *et al.* and a benzyl alcohol solvent as taught by Uchikawa *et al.*, one skilled in the art would have no motivation to modify the formulation by removing the requirement for a cyclodextrin, which not only represents an essential element of Navarro *et al.*, but would also renders the formulation unsatisfactory for its intended purpose. Further, based upon the teaching of Navarro *et al.* that it is the **combination** of cyclodextrin and minoxidil that imparts improved solubility properties to minoxidil while reducing the amount of solvent needed, one skilled in the art would not have had any reasonable expectation that modifying the formulation of Navarro *et al.* to include an acid salt of minoxidil and a benzyl alcohol solvent **while removing** the requisite cyclodextrin would be successful. In view of the foregoing, Applicants respectfully request that the Examiner withdraw the rejection.

E. Di Schiena in view of Weiner *et al.*

The Examiner has rejected claims 1-3, 5-6, 8-9, 12-19, and 21-23 as allegedly being obvious over Di Schiena (U.S. 4,866,067) in view of Weiner *et al.* In the Office Action, the Examiner states that a proper comparison of Di Schiena and the inventive formulation cannot be made since Applicants have not provided the components of the inventive formulation (*see*, page 15 of the Office Action dated May 16, 2005). In response, Applicants respectfully traverse the rejection.

As the Examiner is aware, Applicants can rebut a *prima facie* case of obviousness by presenting comparative test data showing that the claimed invention possesses unexpectedly improved properties or properties that the prior art does not possess. *In re Dillon*, 16 U.S.P.Q. 1897, 1901 (Fed. Cir. 1990). In this regard, the Examiner's attention is respectfully directed to the Declaration of Mr. Albert Zorko Abram under 37 C.F.R. § 1.132 submitted on July 21, 2003 ("the 2003 Declaration"). In the 2003 Declaration, Mr. Abram explained that after mixing the constituent parts of the comparative foam formulation (*i.e.*, the Di Schiena formulation of

Example 3(e)), the resulting mixture was brown in color and separated into two phases (*i.e.*, biphasic) upon standing (*see*, paragraph 13 of the 2003 Declaration). In stark contrast, Mr. Abram declared that after mixing the constituent parts of the inventive foam formulation, the resulting mixture was a clear and colorless single-phase (*i.e.*, homogeneous) solution (*see*, paragraph 14 of the 2003 Declaration). The **homogeneous** nature of the inventive formulation had several **unexpected advantageous properties** that were not present in the **heterogeneous** comparative formulation, including foam consistency, uniformity of dosing, foam color, foam stability, and advantageous mechanical shear properties (*see*, paragraphs 15-28 of the 2003 Declaration).

Although Applicants believe that the side-by-side comparative evidence presented in the 2003 Declaration is more than sufficient to rebut any *prima facie* case of obviousness, to remove all doubt that the components of the inventive formulation have been fully disclosed, Applicants submit herewith a copy of a Declaration of Mr. Abram under 37 C.F.R. § 1.132 ("the 2004 Declaration"), first submitted in a continuation application (Patent Application No. 10/124,197) of the subject case. As explained by Mr. Abram in the 2004 Declaration, the inventive foam was prepared according to the formulation set forth in the table in paragraph 8 (*see also*, Exhibit B). For the Examiner's convenience, this table is reproduced below:

Component	% w/w
Minoxidil	4.75
Ethanol	53.645
Purified Water	31.410
Butylated Hydroxytoluene	0.095
Lactic Acid (90%)	1.00
Citric Acid	0.10
Stearyl Alcohol	0.50
Cetyl Alcohol	1.10
Polysorbate 60	0.40
Propylene Glycol	2.00
Propellant P70	5.00
Total	100.00

Applicants assert that this table clearly shows the identity ("Component") and amount ("% w/w") of each and every component in the inventive formulation used for the side-by-side comparison. As such, Applicants have provided, in the form of the 2003 Declaration and the 2004 Declaration, a side-by-side comparison of the inventive formulation against the Di Schiena comparative formulation that is effective to rebut a *prima facie* case of obviousness because Applicants have shown that the claimed invention possesses unexpectedly improved solution and mechanical properties over Di Schiena.

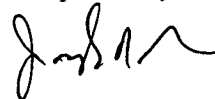
In view of the unexpected and surprising results, Applicants submit that Di Schiena does not present a bar under 35 U.S.C. § 103(a), either alone or in combination with Weiner *et al.*, to the patentability of the present invention. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

#### IV. CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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